

### REMARKS

Claims 1 – 10, 13 – 24, and 27 – 34 are pending in the instant patent application. Claims 11 – 12 and 25 – 26 have been withdrawn as the result of an earlier restriction requirement.

Claims 2 – 3, 5 – 7, 14 – 15, and 17 – 19 have been amended to overcome the objections cited in the Office Action. Withdrawal of the objections is respectfully requested.

Claims 1 – 10, 13 – 34, and 27 – 34 have been rejected under 35 U.S.C. § 101 as being directed to non-statutory subject matter. Specifically, the Office Action asserts that the rejected claims are “merely a mathematical manipulation of data” that “is equivalent to a mental process.” Furthermore, the Office Action appears to assert that the rejected claims do not “produce a result which is concrete, tangible, and useful.

Applicants agree with the Office Action that the pending claims are directed to a method of “estimating the effects of factors and interactions between factors in a gene microarray experiment” but respectfully submit that the pending claims are drawn to statutory subject matter for the following reasons.

The Office Action appears to base its assertion that the rejected claims do not produce a concrete, tangible, and useful result on the fact that the rejected claims do not identify specific factors or effects. This position is reinforced by the statement that no “correlation to a known disease or disorder is recited in the claims.”

The scope of the applicants' invention, however, is broader than a single set of factors and effects. No correlation to a known disease or disorder is recited in the claims because the claimed methods may be used to find such correlations once the experimenter has defined his/her experiment design. Whether the experimenter is trying to determine differential gene expression for diabetes or breast cancer, for

example, the claimed methods may be used to identify such correlations, which are concrete, tangible and useful.

Claims 1 – 10, 13 – 34, and 27 – 34 have been rejected under 35 U.S.C. § 101 because the claimed invention lacks patentable utility. In support of this rejection, the Office Action asserts that the rejected claims “would not have a utility as further research would be required to determine what the effect IS.”

In response, Applicants submit that one of skill in the art would appreciate that the Applicants' invention does not stand in isolation but is part of a broader context usually referred to as a designed experiment. A designed experiment may be partitioned into three stages. The first stage defines the goal of the experiment, identifies the independent and dependent variables of the experiment and designs the experimental procedures. The second stage performs the experiment according to the designed procedures and measures and records the responses (independent variables). The third stage analyzes the recorded responses from which a conclusion may be drawn. Each stage must be run in sequential order. For example, it is impossible to analyze the data before it is collected. Similarly, one cannot analyze the data before the experiment is designed or before the identification of the dependent and independent variables, which appears to be the basis of the Office Action's utility rejection. One of skill in the art, however, would know that prior to performing the statistical data analysis of the third phase, the experiment goal and dependent and independent variables have already been identified.

Contrary to the Office Action's statement, the third phase does determine what the effect is and this is where Applicants' invention is useful and produces a concrete and tangible result. One of skill in the art should appreciate that the measured fluorescent light intensities from gene expression microarrays contain a significant amount of variation and that conclusions directly based on the raw microarray data are highly suspect. Applicants' invention enables an experimenter to “clean up” the raw microarray data such that statistically valid conclusions can be made. Using an analogy from the electrical arts, the raw microarray data contains a lot of noise from the

uncontrollable variations of the microarray experiment and Applicants' invention essentially filters the raw signal to remove the noise from the signal. In other words, Applicants' invention can partition the spot light intensity (raw data or dependent variable) into portions attributable to each (the effect) of the factors and interactions (independent variables). See Applicants' Specification, p. 4, line 22 to p. 5, line 4.

Applicants submit that one of skill in the art would immediately recognize the usefulness of the rejected claims and appreciate that the identification of the dependent and independent variables is known at the time of application of the claimed invention. Therefore, Applicants respectfully request that the utility rejections be withdrawn.

Claims 1 – 10, 13 – 34, and 27 – 34 have been rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the enablement requirement because “the instant specification nor the prior art teach how to determine effects of factors and interactions on an unknown entity.”

In response, Applicants respectfully submit that one of ordinary skill in the art, which we agree is a high level, would understand that prior to using the methods described in Applicants' specification, the person would first have to design the experiment by, *inter alia*, identifying the factors, independent variables, and the goal of the design. For example, experimenter A may choose to include the dye as one of the factors in his/her design A while experimenter B may choose not to include the dye as a factor in his/her design B. The decision to include or exclude a variable depends on many things, such as the goal of the experiment, time, cost, availability of materials, etc., that an experimenter is expected to know and appreciate. Applicants' claimed invention, however, is not directed to the design of experiments but is directed to a method of “estimating the effects of factors and interactions between factors in a gene microarray experiment”. The scope of Applicants' invention covers both design A and B. In design A, Applicants' claimed method may be used to determine the effect of dye on measured light intensities of the microarray experiment. In design B, Applicants' claimed method cannot estimate the effect of dye because the dye variable was not

identified or incorporated into design B. The claimed method, however, may still be used to estimate the effects of the other factors identified in design B.

The scope of Applicants' invention is broad enough to cover any choice or combination of factors in a microarray experiment but this does not mean that the factors are unknown to the experimenter. In the broad context of a designed experiment, the factors are selected during the experiment design and prior to the performance of the actual experiment. One of skill in the art is expected to know how to design a proper microarray experiment and therefore will have selected and know the factors for the designed experiment.

Similarly, during the design of a microarray experiment, one of skill in the art must decide, prior to the use of the claimed methods, the goal of the experiment. For example, Applicants' specification states on page 2, lines 8 – 10, that "the purpose of a typical cDNA microarray experiment is to determine the effect, if any, between the genes on the microarray and the labeled cDNA samples." Therefore, if one of skill in the art is designing a cDNA microarray experiment, that person identifies the effects that are sought by selecting the factors in the experiment. After the experiment is performed and the fluorescent light intensities for each spot recorded, the methods of the Applicants' invention may be employed to determine the effect, if any, between the genes on the microarray and the labeled cDNA samples. As with other statistical methods of data analysis, the factors and the hypothesized effects or correlations are already identified prior to the statistical data analysis.

Applicants respectfully submit that the lack of enablement rejections have been overcome and request that these rejections be withdrawn.

Claims 1 – 10, 13 – 34, and 27 – 34 have been rejected under 35 U.S.C. § 112, second paragraph as failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In response, claims 1 and 13 have been amended to more clearly indicate that a gene expression microarray experiment generates a microarray dataset. Claims 3, 14,

and 15 have been amended to more clearly state that each factor is characterized by a number of levels.

Applicants respectfully submit that the 35 U.S.C. § 112, second paragraph rejections have been overcome and request that these rejections be withdrawn.

Replacement drawings sheets are attached. Drawing sheet 1 containing Fig. 1 and drawing sheet 2 containing Fig. 2, have been amended to correct informalities of the originally submitted drawings. No new matter has been added.


The Office Action objects to the Applicants' specification because it contains embedded hyperlink or browser-executable code. In response, Applicants assert that no active embedded hyperlink or browser-executable code was contained in the original application *papers* filed on May 25, 2001. The hyperlinks cited by the Office Action are included to comply with the requirements of 35 U.S.C. § 112 and are not intended to be active links. See MPEP § 801.1 and § 707.05(e).

Applicants respectfully request entry of the foregoing amendments and remarks into the file history of the above-identified application. Applicants believe that each ground for rejection has been successfully overcome and/or obviated, and that all pending claims are in condition for allowance. Withdrawal of the rejections and allowance of the application are respectfully requested.

No additional fee is believed to be due in connection with filing of the instant request. However, if a fee is due, please charge the required fee to Morgan, Lewis & Bockius LLP Deposit Account No. 50-0310.

Respectfully submitted,

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Attachments